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| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.  | CONFIRMATION NO. |
|---|-------------|----------------------|----------------------|------------------|
| 10/647,382  | 08/26/2003  | Imran Ahmed          | 033388-566           | 2045             |
| 23117   | 7590        | 04/01/2005           | EXAMINER             |                  |
| NIXON & VANDERHYE, PC<br>1100 N GLEBE ROAD<br>8TH FLOOR<br>ARLINGTON, VA 22201-4714 |             |                      | KISHORE, GOLLAMUDI S |                  |
|   |             |                      | ART UNIT             | PAPER NUMBER     |
|   |             |                      | 1615                 |                  |

DATE MAILED: 04/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                            |                     |
|------------------------------|----------------------------|---------------------|
| <b>Office Action Summary</b> | <b>Application No.</b>     | <b>Applicant(s)</b> |
|                              | 10/647,382                 | AHMED ET AL         |
|                              | <b>Examiner</b>            | <b>Art Unit</b>     |
|                              | Gollamudi S. Kishore, Ph.D | 1615                |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) Responsive to communication(s) filed on 15 December 2004.
- 2a) This action is FINAL.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-23 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____ .  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>3-14-05</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|  | 6) <input type="checkbox"/> Other: _____                                    |

## DETAILED ACTION

The amendment dated 12-15-04 is acknowledged. Claims included in the prosecution are 1-23.

### ***Double Patenting***

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1-23 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 6,667,053. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claim 1 recites a liposome containing an optically active ether lipid component and encompasses the liposomes in patented claims which contain the same ether lipids and other bilayer components PC, sterol and PE linked to a dicarboxylic acid. The same is the case with instant method of treatment claims and the patented claims.

3. Claims 1-23 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,180,137. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claim 1 recites a liposome containing an optically active ether lipid component and encompasses the liposomes in patented claims which contain a specific ether lipid and other bilayer components PC, sterol and PE linked to a dicarboxylic acid. Instant method of treatment of cancer includes various cancers recited in the patented claims.

4. Claims 1-18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 5,965,159. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claim 1 recites a liposome containing an optically active ether lipid component and encompasses the liposomes in patented claims which contain a specific ether lipid and other bilayer components PC, sterol and PE linked to a dicarboxylic acid.

5. Claims 1-23 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 5,762,958. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claim 1 recites a liposome containing an optically active ether lipid component and encompasses the liposomes in patented claims which contain a specific ether lipid and other bilayer components PC, sterol and

PE linked to a dicarboxylic acid. Similar is the case with instant method claims and the patented method claims.

6. Claims 19-23 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 6,017,557. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant method claim 19 recites a liposome containing an optically active ether lipid component and encompasses the liposomes in patented method claims which contain a specific ether lipid and other bilayer components PC, sterol and PE linked to a dicarboxylic acid. Instant specific cancers are deemed to be included in generic 'cancer' in patented claim 1.

7. Claims 1-18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 5,932,242. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claim 1 recites a liposome containing an optically active ether lipid component and encompasses the liposomes in patented claims which contain a specific ether lipid and other bilayer components PC, sterol and PE linked to a dicarboxylic acid.

The above double patenting rejections are maintained since no terminal disclaimers have been filed.

***Claim Rejections - 35 USC § 102***

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 4, 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 93/08202 of record.

WO discloses liposomes containing ether lipids (note the abstract, page 25 and the claims).

10. Claims 1, 3, 13, 14 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by TAKE (JP 61 22-020 A).

TAKE discloses liposomes containing claimed anti-tumor ether lipid (note abstract).

11. Claims 1, 3, 13, 14 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Mende et al (Pharmazie, 1989) of record.

Mende et al disclose liposomes containing ether lipid, ET-18-OCH<sub>3</sub> (note abstract).

Applicant's arguments to the above rejections have been fully considered, but are not found to be persuasive. Applicant argues that instant claim 1 now is amended to recite 'consisting essentially of' and none of the references teach such a liposome. This argument is not found to be persuasive. When applicant contends that modifying components in the reference composition are excluded by the recitation of "consisting essentially of" applicant has burden of showing the basic and novel characteristics of his

composition – i.e., a showing that the introduction of these components would materially change the characteristics of applicant's composition (*In re De Lajarte*, 337 F 2d 870, 143 U.S.P.Q. 256 (C.C.P.A. 1964)). In instant case, applicant has not shown any unexpected results or novel Characteristics obtained by removing the D form of the ether lipid (ether lipid is a broad term) from the recemic mixture.

*Claim Rejections - 35 U.S.C. § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1, 3-4, 13-14 and 17-22 are rejected under 35 U.S.C. § 103 as being unpatentable over TAKE cited above.

As pointed out above, TAKE discloses liposomes containing claimed anti-tumor ether lipid (note abstract). TAKE does not specifically teach whether the ether lipid is in a specific optical isomer form. However, since TAKE teaches that the ether lipid is an anti-tumor ether lipid, in the absence showing otherwise, it is deemed obvious to one of ordinary skill in the art that both D and L forms of the compound or a mixture would possess the anti-tumor property. TAKE does not appear to teach the amount of the composition to be administered for cancer treatment. However, it is deemed that the amounts are manipulatable parameters since they depend upon a variety of factors

including the nature of cancer, the age of the patient and the severity of the disease.

TAKE does not teach the inclusion of an additional active agent or additional chemotherapeutic agent. Since combination therapy is commonly practiced in cancer treatment, it is deemed obvious to one of ordinary skill in the art to include an additional agent with the expectation of obtaining at least an additive effect.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant's only argument is that the examiner has provided no basis to support the assertion that it would be obvious that both D and L forms of ether lipid, or a mixture would possess anti-tumor activity. This argument is not found to be persuasive. As pointed out above, when applicant contends that modifying components in the reference composition are excluded by the recitation of "consisting essentially of" applicant has burden of showing the basic and novel characteristics of his composition – i.e., a showing that the introduction of these components would materially change the characteristics of applicant's composition (*In re De Lajarte*, 337 F 2d 870, 143 U.S.P.Q. 256 (C.C.P.A. 1964)). In instant case, applicant has not shown any unexpected results or novel Characteristics obtained by removing the D form of the ether lipid (ether lipid is a broad term) from the recemic mixture. The examiner also cites in this context, the reference of Thiele (4,182,902), which shows that both D and L forms, as well as recemates of p-(p-chlorobenzyl)phenoxyacetic acids possess hypocholesterolemic and hypolipemic activity (col. 3, line 50 et seq.). The reference of Pieringer (5,444,052) which shows optical isomers of glycerol ethers are equally effective in their activity is also cited of interest (Figures 11 and 12 and col. 8, line 65 et seq.).

13. Claims 1, 4, 17 and 18 are rejected under 35 U.S.C. § 103 as being unpatentable over WO 93/08202 cited above.

As pointed out above, WO discloses liposomes containing ether lipids (note the abstract, page 25 and the claims). Although WO does not specifically teach whether the ether lipid is in specific optical isomer form, it would have been obvious to one of ordinary skill in the art that one could use either L form or D form in the formation of liposomes with a reasonable expectation of success.

14. Claims 1, 3, 13, 14 and 18 are rejected under 35 U.S.C. § 103 as being unpatentable over Mende et al (Pharmazie, 1989).

As pointed out above, Mende et al disclose liposomes containing ether lipid, ET-18-OCH<sub>3</sub> (note abstract). Although Mende et al do not specifically teach whether the ether lipid is in specific optical isomer form, it would have been obvious to one of ordinary skill in the art that one could use either L form or D form in the formation of liposomes of Mende with a reasonable expectation of success.

15. Claims 1-22 are rejected under 35 U.S.C. § 103 as being unpatentable over TAKE cited above, in combination with Schroit (4,983,397) of record.

The teachings of the TAKE have been discussed above. What is lacking in TAKE is the inclusion in the liposomes of a lipid derivatized with a dicarboxylic acid.

Schroit teaches that when amine lipids, which are derivatized with dicarboxylic acids, are used in combination with other phospholipids in a liposomal form, then the uptake of those liposomes (also containing drugs) by endocytosis by macrophages is surprisingly increased (note the abstract; columns 1-2 and claims).

The inclusion of a lipid derivatized with a dicarboxylic acid in the liposomes formed from ether lipids would have been obvious to one of ordinary skill in the art because of Schroit's teachings of increased uptake of the liposomes. TAKE in addition to the ether lipids teaches the inclusion of several phospholipids, which form the liposomal bilayer. These include phosphatidylcholine (PC) and phosphatidylethanolamine (PE) with stearic acid or palmitic acids as the fatty acid moieties. Although TAKE does not specifically teach instant fatty acids in phosphatidylethanolamine, since these are art known phospholipids in liposome formation, it is deemed obvious to one of ordinary skill in the art to select PE and PC with desired fatty acids with a reasonable expectation of success.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that the primary reference does not teach the liposome as claimed and nothing in the secondary reference cures this fundamental failing. This argument has been addressed above. Applicant provides no specific arguments with regard to the secondary reference.

16. Claims 17 and 20-22 are rejected under 35 U.S.C. § 103 as being unpatentable over TAKE, in combination with Schroit (4,983,397) as set forth above, in further combination with Bissery (5,908,835).

The teachings of TAKE have been discussed above. What is lacking in TAKE is the teaching of the inclusion of additional anti-cancer agent.

Bissery teaches that compositions can be formulated to include two or more chemotherapeutic drugs to practice combination therapy and to obtain greater than the expected additive effect (abstract, col. 1, lines 28-53 and claims).

To include additional chemotherapeutic drugs in the teachings of TAKE and Schroit would have been obvious to one of ordinary skill in the art since Bissery teaches that Bissery teaches that compositions can be formulated to include two or more chemotherapeutic drugs to practice combination therapy and to obtain greater than the expected additive effect.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant once again argues that the primary reference does not teach the liposome as claimed and nothing in the secondary reference cures this fundamental failing. This argument has been addressed above. Applicant provides no specific arguments with regard to the secondary reference.

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

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extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Gollamudi S Kishore, Ph.D  
Primary Examiner  
Art Unit 1615

GSK